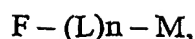


**Patent Claims**

1. A fusion protein of the structure



- 5 having essentially the same biological specificity and activity of human TPO, comprising an immunoglobulin heavy chain constant region (F) and a human TPO molecule (M) in a truncated (1 – 174) form modified by one or more amino acid substitutions, wherein said fusion protein is substantially non-immunogenic or less immunogenic than the parental fusion protein comprising the non-modified human TPO, and said amino acid substitutions  
10 have been carried out in one or more of the sequence tracks

(i) GEWKTQMEETKAQDILGAVTLLLEGVM,

(ii) PTTAVPSRTSLVLTLL

- within the truncated wild-type TPO molecule and cause a reduction or an elimination of one or more of T-cell epitopes, which act in the parental non-modified fusion molecule as  
15 MHC class II binding ligands and stimulate T-cells, said immunoglobulin heavy chain constant region is fused directly ( $n = 0$ ) or indirectly ( $n = 1$ ) via a linker molecule (L) to said modified human TPO molecule (M).

2. A fusion protein according to claim 1, wherein F is an Fc domain.

3. A fusion protein of claim 1 or 2, wherein F comprises a hinge region.

4. A fusion protein according to any of the claims 1 – 3, wherein the C-terminus of the human immunoglobulin heavy constant region domain is linked directly or indirectly to the N-  
25 terminus of the modified TPO molecule.

5. A fusion protein according to any of the claims 1 – 4, wherein said modified TPO molecule contains one or more of the amino acid substitutions  
M55K, A60R and V161A  
30 within the sequence tracks (i) – (ii).

6. A fusion protein according to any of the claims 1 – 4, wherein said TPO molecule in said fusion protein has the formula / structure:

SPAPPACDLRLVLSKLLRDSHVLHSRLSQCPVHPLPTFVLLPAVDFSLGX<sup>1</sup>X<sup>2</sup>KTQX<sup>3</sup>EEX<sup>4</sup>KX<sup>5</sup>X<sup>6</sup>D  
 X<sup>7</sup>LGAX<sup>8</sup>TX<sup>9</sup>LX<sup>10</sup>X<sup>11</sup>GVMAARGQLGPTCLSSLLGQLSGQVRLLLGALQSLTQLPPQGRTTAHKDP  
 NAIFLSFQHLRLRGKVRFLMLVGGSTLCVRRAPPTTAX<sup>12</sup>X<sup>13</sup>SRTSLVLTNL

X<sup>1</sup> is A, E;

5 X<sup>2</sup> is S, W;

X<sup>3</sup> is A or T or K, S or M;

X<sup>4</sup> is A, T;

X<sup>5</sup> is R, A;

X<sup>6</sup> is A or T or Q;

10 X<sup>7</sup> is A or T or I;

X<sup>8</sup> is A or T or V;

X<sup>9</sup> is A or T or S or L;

X<sup>10</sup> is A or L;

X<sup>11</sup> is A or S or E;

15 X<sup>12</sup> is N or A or T or R or E or D or G or H or P or K or Q or V;

X<sup>13</sup> is A or P,

and whereby simultaneously X<sup>1</sup> = E, X<sup>2</sup> = W, X<sup>3</sup> = M, X<sup>4</sup> = T, X<sup>5</sup> = A, X<sup>6</sup> = Q, X<sup>7</sup> = I,  
 X<sup>8</sup> = V, X<sup>9</sup> = L, X<sup>10</sup> = L, X<sup>11</sup> = E, X<sup>12</sup> = V and X<sup>13</sup> = P are excluded.

20 7. A fusion protein according to any of the claims 1 – 6, wherein F is in Fc domain of human IgG4.

8. A fusion protein according claim 7, wherein L is a peptide linker having 4 – 20 amino acid residues.

25

9. A fusion protein according to any of the claims 1 – 8, selected from the group consisting of  
 F – M1 to F – M67,

F – L – M1 to F – L – M67, and

F1 – L – M1 to F1 – L1 – M67,

30

wherein F is an immunoglobulin heavy chain constant region, L is a linker peptide, F1 is a Fc domain of human IgG4 comprising a modified hinge region, L1 is a peptide linker having the sequence GAGGGGSGGG GSGGGSG, and M1 – M67 are modified TPO sequences as specified in Table A1.

10. A fusion protein according to claim 9 selected from the group consisting of  
F - M1, F - L - M1, F1 - L1 - M1  
F - M66, F - L - M66, F1 - L1 - M66, and  
F - M67, F - L - M67, F1 - L1 - M67.
- 5
11. A dimeric fusion protein comprising two identical monomeric fusion protein chains according to any of the claims 1 - 10.
12. A peptide molecule selected from the group consisting of
- 10 (i) GEWKTQMEETKAQDILGAVTLLLEGVM,  
(ii) PTTAVPSRTSLVLT
- or a sequence track consisting of at least 9 consecutive amino acid residues of any of said peptide molecules having a potential MHC class II binding activity and created from the primary sequence of non-modified human TPO, whereby said peptide molecule or
- 15 sequence track has a stimulation index of  $> 1.8$  in a biological assay of cellular proliferation and said index is taken as the value of cellular proliferation scored following stimulation by a peptide and divided by the value of cellular proliferation scored in control cells not in receipt peptide.
- 20 13. Use of a peptide molecule according to claim 12 for the manufacture of a vaccine in order to reduce immunogenicity to TPO in a patient.
14. A peptide molecule modified by one or more amino acid substitutions deriving from any peptide molecule according to claim 11 and having a reduced or absent potential MHC
- 25 class II binding activity expressed by a stimulation index of less than 2, whereby said index is taken as the value of cellular proliferation scored following stimulation by a peptide and divided by the value of cellular proliferation scored in control cells not in receipt peptide.
15. Use of a modified peptide molecule according to claim 14 for the manufacture of a modified TPO molecule M1 to M67 of Table A1, or a fusion protein comprising an Fc
- 30 portion of an immunoglobulin and said modified TPO molecule.